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AMENDMENT AFTER FINAL 11/19/03
EXPEDITED PROCEDURE
ART UNIT 1632
U.S.S.N. 09/750,779
12013/55202

AMENDMENTS TO THE CLAIMS:

1. (Currently Amended) An implantable medical device comprising a coating on at least a portion thereof , said coating comprising:

an inner layer of a cationic polyelectrolyte carrier; and

a layer of at least one negatively charged therapeutic agent adsorbed onto said inner layer of cationic polyelectrolyte carrier; and

an additional layer or layers of cationic polyelectrolyte carrier and an additional layer or layers of at least one negatively charged therapeutic agent adsorbed onto said additional layer or layers of cationic polyelectrolyte carrier, wherein said additional layer or layers of polyelectrolye carrier and said additional layer or layers of at least one negatively charged therapeutic agent alternate.

2. (Original) The medical device of claim 1, further comprising an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner or additional layer or layers of cationic polyelectrolyte carrier.

3. (Currently Amended) The medical device of claim 2, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner or additional layer or layers of polyelectrolyte carrier.

4. (Currently Amended) The medical device of claim 1, wherein at least one of the inner or additional layer of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

5. (Original) The medical device of claim 1, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

6. (Cancelled).

7. (Currently Amended) The medical device of claim 1, wherein the at least onenegatively charged therapeutic agent comprises rapamycin.

8. (Currently Amended) The medical device of claim 1, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

9. (Cancelled)

10. (Currently Amended) A method of adsorbing at least one negatively charged therapeutic agent onto a medical device comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;

(b) washing the inner layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the inner layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

11. (Currently Amended) The method of claim 10, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

12. (Original) The method of claim 11, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of polyelectrolyte carrier.

13. (Original) The method of claim 10, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises a human serum albumin, gelatin, chitosan, or a combination thereof.

14. (Original) The method of claim 10, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

15. (Cancelled).

16. (Currently Amended) The method [medical device] of claim 10, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

17. (Currently Amended) The method [medical device] of claim 10, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

18. (Cancelled)

19. (Currently Amended) A medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion thereof and produced by a process comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form an inner layer of cationic polyelectrolyte carrier;

(b) washing the inner layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the inner layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

20. (Currently Amended) The medical device of claim 19, wherein the process further comprises the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

21. (Original) The method of claim 20, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

22. (Original) The medical device of claim 19, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

23. (Original) The medical device of claim 19, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

24. (Cancelled)

25. (Currently Amended) The medical device of claim 19, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

26. (Currently Amended) The medical device of claim 19, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

27. (Cancelled)

28. (Currently Amended) A method of delivering a therapeutic agent to a target location by implanting in the target location a medical device comprising at least one negatively charged therapeutic agent adsorbed on at least a portion thereof; wherein the medical device is produced by a process comprising:

(a) coating at least a portion of a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(b) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of

cationic polyelectrolyte carrier and therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

29. (Currently Amended) The method of claim 28, further comprising the step of coating the outermost layer of the at least one negatively charged therapeutic agent with an outermost layer of a cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

30. (Original) The method of claim 29, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

31. (Original) The method of claim 28, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

32. (Original) The method of claim 28, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

33. (Cancelled)

34. (Currently Amended) The method of claim 28, wherein the at least one negatively charged therapeutic agent comprises rapamycin.

35. (Currently Amended) The method of claim 28, wherein the at least one negatively charged therapeutic agent comprises paclitaxel.

36. (Cancelled)

37. (Previously Amended) The method of claim 28, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

38. (Currently Amended) A method for treating the occurrence or severity of a clinical disease or condition, comprising:

(a) preparing a medical device by:

(i) coating at least one a portion of a medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to treat or reduce the occurrence of the clinical disease or condition onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into a target location in a mammal from which the at least one negatively charged therapeutic agent can treat or reduce the occurrence or severity of the clinical disease or condition.

39. (Currently Amended) The method of claim 38, further comprising the step of coating the outermost layer of at least one negatively charged therapeutic agent with an outermost layer of cationic polyelectrolyte carrier which is the same or different from the inner layer or multiple layers of cationic polyelectrolyte carrier.

40. (Original) The method of claim 39, wherein the outermost layer of cationic polyelectrolyte carrier is more hydrophobic and/or more cationic than at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier.

41. (Original) The method of claim 38, wherein at least one of the inner layer or multiple layers of cationic polyelectrolyte carrier comprises human serum albumin, gelatin, chitosan, or a combination thereof.

42. (Original) The method of claim 38, wherein the medical device comprises a stent, a catheter, a balloon catheter, or a combination thereof.

43. (Cancelled)

44. (Currently Amended) The method of claim 38, wherein the clinical disease or condition comprises restenosis or angiogenesis and theat least one negatively charged therapeutic agent comprises rapamycin.

45. (Currently Amended) The method of claim 38, wherein the clinical disease or condition comprises a malignancy or malignant cell growth and the at least one negatively charged therapeutic agent comprises paclitaxel.

46. (Previously Amended) The method of claim 38, wherein the target location comprises at least one location selected from the group consisting of brain, heart, liver, skeletal muscle, smooth muscle, kidney, bladder, intestines, stomach, pancreas, ovary, prostate, cartilage, bone, lung, blood vessel, ureter, urethra, and testes.

47. (Currently Amended) The medical device of claim 1 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, and a polynucleotide encoding any of the above named proteins or protein inhibitors.

48. (Previously Presented) The medical device of claim 47 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

49. (Currently Amended) The medical device of claim 47 wherein the antioxidant compound is probucol or retinoic acid.

50. (Currently Amended) The method of claim 10 wherein theat least one negatively charged therapeutic agent is selected from the group consisting of: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant,

vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, and a polynucleotide encoding any of the above named proteins or protein inhibitors.

51. (Previously Presented) The method of claim 50 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

52. (Currently Amended) The method of claim 50 wherein the antioxidant compound is probucol or retinoic acid.

53. (Currently Amended) The medical device of claim 19 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agents for treating malignancies, bone morphogenic protein, and a polynucleotide encoding any of the above named proteins or protein inhibitors.

54. (Currently Amended) The medical device of claim 53 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

55. (Currently Amended) The medical device of claim 53 wherein the antioxidant compound is probucol or retinoic acid.

56. (Currently Amended) The method of claim 28 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agent for treating malignancies, bone morphogenic protein, and a polynucleotide encoding any of the above named proteins or protein inhibitors.

57. (Previously Presented) The method of claim 56 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

58. (Currently Amended) The method of claim 56 wherein the antioxidant compound is probucol or retinoic acid.

59. (Currently Amended) The method of claim 38 wherein the at least one negatively charged therapeutic agent is selected from the group consisting of: anti-thrombogenic protein, antioxidant compound, angiogenic protein, agent which blocks smooth muscle cell proliferation, anti-inflammatory agent, calcium entry blocker, antineoplastic/antiproliferative/anti-mitotic compound, anti-microbial compound, anesthetic agent, nitric oxide donor, anti-coagulant, vascular cell growth promoting protein, vascular cell growth protein inhibitor, vascular cell growth antibody inhibitor, cholesterol lowering drug, vasodilating drug, protein that protects

against cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, agentfor treating malignancies, bone morphogenic protein, and a polynucleotide encoding any of the above named proteins or protein inhibitors.

60. (Previously Presented) The method of claim 59 wherein the anti-thrombogenic protein is heparin, heparin derivatives, urokinase, or PPACK.

61. (Currently Amended) The method of claim 59 wherein the antioxidant compound is probucol or retinoic acid.

62. (Currently Amended) A method of delivering a therapeutic agent to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is produced by a process comprising:

(a) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(b) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(c) adsorbing at least one negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(d) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (a) through (c) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device.

63. (Currently Amended) A method of delivering a polynucleotide encoding a protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the at least one negatively charged therapeutic agent has been adsorbed onto the medical device;wherein the at least one negatively charged therapeutic agent is the polynucleotide encoding a protein.

64. (Currently Amended) A method of delivering a DNA encoding a therapeutic protein to a mammal, the method comprising implanting a medical device at a desired location or tissue in a mammal, wherein the medical device is prepared by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of

cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device; wherein the at least one negatively charged therapeutic agents is a DNA encoding a therapeutic protein, wherein the therapeutic protein is selected from the group consisting of anti-thrombogenic protein, angiogenic protein, vascular cell growth promoting protein, vascular cell growth protein inhibitor, protein that protectsagainst cell death, cell cycle CDK protein inhibitor, anti-restenosis protein, and bone morphogenic protein.

65. (Currently Amended) A method for inhibiting restenosis or the growth of tumor cells in a mammal, comprising:

(a) preparing a medical device by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to inhibit restenosis or the growth of tumor cells onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively chargd therapeutic agent until a desired amount of at least one negatively charged therapeutic agent has been adsorbed onto the medical device;

(b) implanting the medical device into a target location in a mammal;

wherein the at least one negatively charged therapeutic agent is a DNA coding for an anti-proliferative protein.

66. (Currently Amended) A method for inducing the growth of blood vessels at a target location in a mammal, comprising:

(a) preparing a medical device by:

(i) coating at least a portion of the medical device with a cationic polyelectrolyte carrier to form a layer of cationic polyelectrolyte carrier;

(ii) washing the layer of cationic polyelectrolyte carrier with a washing solution;

(iii) adsorbing at least one negatively charged therapeutic agent effective to induce the growth of blood vessels onto the layer of cationic polyelectrolyte carrier to form a layer of at least one negatively charged therapeutic agent; and optionally

(iv) washing the layer of at least one negatively charged therapeutic agent with a washing solution and repeating steps (i) through (iii) one or more times to form multiple layers of cationic polyelectrolyte carrier and at least one negatively charged therapeutic agent until a desired amount of the least one negatively charged therapeutic agent has been adsorbed onto the medical device.

(b) implanting the medical device into the target location in a mammal;

wherein the at least one negatively charged therapeutic agent is a DNA coding for an angiogenic protein.

67. (New) The medical device of claim 47, wherein the polynucleotide is inserted into an adenovirus vector.

68. (New) The method of claim 50, wherein the polynucleotide is inserted into an adenovirus vector.

69. (New) The medical device of claim 53, wherein the polynucleotide is inserted into an adenovirus vector.

70. (New) The method of claim 56, wherein the polynucleotide is inserted into an adenovirus vector.